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09/515,806	02/29/2000	William James Cook	381552000200	1012

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EXAMINER
RAMIREZ, DELIA M

ART UNIT	PAPER NUMBER
1652	12

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/515,806	Applicant(s) COOK ET AL.	
	Examiner Delia M. Ramirez	Art Unit 1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10/4/2001* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-30* is/are pending in the application.

4a) Of the above claim(s) *13-21 and 23-30* is/are withdrawn from consideration.

5)☒ Claim(s) 2 is/are allowed.

6)☒ Claim(s) *1,3-12 and 22* is/are rejected.

7)☒ Claim(s) 3 is/are objected to.

8)☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *29 February, 2000* is/are objected to by the Examiner.

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15) ☒ Notice of References Cited (PTO-892)
16) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)
17) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 6 .
18) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
19) ☐ Notice of Informal Patent Application (PTO-152)
20) ☐ Other: .

DETAILED ACTION

Status of the Application

Claims 1-30 are pending.

Applicant's election without traverse of Group I (claims 1-12, 22) drawn to nucleic acids, vectors, host cells encoding and expression of a 14790 kinase in Paper No. 11, filed on 10/4/2001 is acknowledged. Claims 13-21 and 23-30 are hereby withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention.

Specification

1. The drawings have been reviewed and are objected under 37 CFR 1.84 or 1.152. See attached Notice of Draftsperson's Patent Drawing Review.

2. The specification indicates that a biological deposit has been made but there is no indication in the specification as to when the deposited plasmid was publicly available or which accession number was assigned. A biological deposit is not required under 35 USC § 112 in the instant case, however, Applicant is reminded that if such deposit was made under the terms of the Budapest Treaty, then an affidavit or declaration by Applicant, or statement by an attorney of record over his or her signature and registration number, stating that the specific plasmid has been deposited under the Budapest Treaty and that the plasmid will be irrevocably and without restriction or condition released to the public upon the issuance of the patent, would satisfy the deposit requirements.

The deposit statement in the specification, and all claims which refer to the instant plasmid by name, must be amended to include the deposit accession number. These amendments

should be submitted before the payment of the issue fee as an Amendment After Allowance under 37 CFR 1.312. If the amendment is received after the payment of the issue fee the same should be made under the provisions of 37 CFR 1.312 and a petition filed under 37 CFR 1.183 to waive the requirement of 37 CFR 1.312 that the amendment be filed before or with payment of the issue fee—that is, it must be accompanied by a fee in accordance with 37 CFR 1.17(i) and a petition which includes "a showing of good and sufficient reasons why the amendment is necessary and was not earlier presented and why justice requires waiver of the rule").

Claim Objections

3. Claim 3 is objected to because of the following informalities: the instant claim is directed to an isolated nucleic acid molecule selected from a group, however only one member of the group (i.e. (a)) is shown. Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claims 1, 3-6, 12, and 22 (claims 7-11 dependent thereon) are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

5. Claim 1 is indefinite in the recitation of "nucleic acid molecule comprising the coding region of the nucleotide sequence set forth in SEQ ID NO: 1" as it is unclear absent a statement indicating where the coding region is. It is suggested that Applicants clearly indicate the position

within SEQ ID NO: 1 that contains the coding region (i.e. from nucleotide # to nucleotide # of SEQ ID NO: 1).

6. Claim 3 is indefinite in the recitation of "a nucleic acid molecule comprising the nucleotide sequence contained in the plasmid" because it is not clear which nucleic acid molecule is being claimed without a sequence identifier. There is an infinite number of "nucleotide sequences" in a plasmid, therefore, one of ordinary skill in the art would not know which nucleic acid molecule is being claimed. It is suggested that Applicants clearly define the nucleotide sequence with a sequence identifier.

7. Claim 3 is indefinite in the recitation of "the plasmid deposited with ATTC as Accession Number____" because it is unclear which plasmid is being referred to without the accession number. It is suggested that Applicants indicate the accession number of the instant plasmid.

8. Claim 4 is indefinite in the recitation of "hybridizes to a nucleic acid molecule" and "the coding region of SEQ ID NO: 1" for the following reasons. First, it is unclear which molecule is being claimed without a statement of the conditions under which the hybridization reaction is performed. Nucleic acids which will hybridize under some hybridization conditions will not necessarily hybridize under different conditions. It is suggested that Applicant clearly indicate in the claim which "stringent" hybridization and wash conditions are being used. Secondly, it is unclear which molecule is being claimed without a statement indicating the location of the coding region within SEQ ID NO: 1. It is suggested that Applicants clearly indicate the position within SEQ ID NO: 1 that contains the coding region (i.e. from nucleotide # to nucleotide # of SEQ ID NO: 1).

9. Claim 5(a)-5(b) is indefinite in the recitation of "the coding region of SEQ ID NO: 1" as it is unclear absent a statement indicating the location of the coding region within SEQ ID NO: 1. It is suggested that Applicants clearly indicate the position within SEQ ID NO: 1 that contains the coding region (i.e. from nucleotide # to nucleotide # of SEQ ID NO: 1).

10. Claim 6 is indefinite in the recitation of "hybridizes to a nucleic acid molecule" as it is unclear which molecule is being claimed without a statement of the conditions under which the hybridization reaction is performed. Nucleic acids which will hybridize under some hybridization conditions will not necessarily hybridize under different conditions. It is suggested that Applicants clearly indicate in the claim which "stringent" hybridization and wash conditions are being used.

11. Claim 12 is indefinite in the recitation of "a method of producing a polypeptide" because it is unclear from the claim, as written, as to the identity of the polypeptide being produced. The host cell of claim 12 is capable of producing a large number of polypeptides, both native and recombinant. It is suggested that Applicants clearly define their intended polypeptide.

12. Claim 22 is indefinite in the recitation of "which selectively hybridizes to a nucleic acid molecule" as it is unclear which molecule is being claimed without a statement of the conditions under which the hybridization reaction is performed. Nucleic acids which will hybridize under some hybridization conditions will not necessarily hybridize under different conditions. It is suggested that Applicants clearly indicate in the claim which hybridization and wash conditions are being used.

13. Claim 12 is rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP

§ 2172.01. The claim is directed to a method of producing a polypeptide, however, the only step described in the claim is that of culturing a host cell capable of expressing said polypeptide. There is no step indicating how the polypeptide is being produced or recovered once the host cell is cultured in an appropriate medium.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

14. Claims 4-5 (claims 6-12, 22 dependent thereon) are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claim 4 is directed to a genus of isolated nucleic acid molecules which encode naturally occurring allelic variants of a polypeptide comprising the amino acid sequence of SEQ ID NO: 2. The specification indicates that such allelic variants include functional and non-functional 14790 proteins and that all variants with functional activity are within the scope of the claim (page 15 of the specification). The specification does not provide any description of which positions can be altered without loss of protein activity or which positions would render a non-functional protein. Furthermore, no examples of any of these variants is provided. No information, beyond the characterization of the polypeptide of SEQ ID NO: 2 has been provided by Applicant which would indicate possession of the claimed genus of polynucleotides. The specification only discloses a single species of the claimed genus which is insufficient to put one

of skill in the art in possession of the attributes and features of all species within the claimed genus. Thus, one skilled in the art cannot reasonably conclude that Applicant had possession of the claimed invention at the time the instant application was filed.

Claim 5 is directed to nucleic acid molecules at least 60% homologous to SEQ ID NO: 1, nucleic acid molecules comprising a fragment of at least 200 nucleotides of a nucleic acid comprising the nucleotide of SEQ ID NO: 1, nucleic acid molecules encoding a polypeptide at least 60% homologous to the polypeptide of SEQ ID NO: 2, and nucleic acid molecules encoding a fragment of a polypeptide comprising at least 15 contiguous amino acid residues of the polypeptide of SEQ ID NO: 2. No description has been provided by Applicant of the polynucleotide variants encompassed by the claim. No information, beyond the characterization of the polypeptide of SEQ ID NO: 2 has been provided by Applicant which would indicate possession of the claimed genera of polynucleotides. The specification has no disclosure of the function of (1) all the variants of the polypeptides encoded by the nucleic acid molecules of SEQ ID NO: 1 which have at least 60% sequence identity, (2) all the polypeptides encoded by at least 200 nucleotides of a nucleic acid comprising the nucleotide of SEQ ID NO: 1, and (3) all the polypeptides of at least 15 contiguous amino acid residues of SEQ ID NO: 2. Each genus of polynucleotides claimed is a large variable genus including nucleic acid molecules encoding polypeptides which can have a wide variety of functions. Van de Loo et al. (Proc. Natl. Acad. Sci. 92:6743-6747, 1995) teaches that polypeptides of approximately 67% homology to a desaturase from Arabidopsis where found to be hydrolases once tested for activity. Similarly, Broun et al. (Science 282:1315-1317, 1998) teaches that as few as four amino acid substitutions can convert an oleate 12-desaturase into a hydrolase and as few as six amino acid substitutions

can transform a hydrolase into a desaturase. Therefore, many functionally unrelated polypeptides are encompassed within the scope of the claims. The specification only discloses a single species of the claimed genera which is insufficient to put one of skill in the art in possession of the attributes and features of all species within the claimed genera. Thus, one skilled in the art cannot reasonably conclude that Applicant had possession of the claimed invention at the time the instant application was filed.

15. Claim 4 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the polypeptide of SEQ ID NO: 2, does not reasonably provide enablement for any naturally occurring allelic variant or homolog of the polypeptide of SEQ ID NO: 2. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The criteria for undue experimentation, summarized in *re Wands*, 8, USPQ2nd 1400 (Fed. Cir. 1988) are: 1) quantity of experimentation necessary, 2) the amount of direction or guidance presented, 3) the presence and absence of working examples, 4) the nature of the invention, 5) the state of prior art, 6) the relative skill of those in the art, 7) the predictability or unpredictability of the art, and 8) the breath of the claims.

Since the amino acid sequence of a polypeptide determines its structural and functional properties, predictability of which changes can be tolerated in a polypeptide's amino acid sequence to obtain the desired activity requires knowledge of and guidance with regard to which amino acids, if any, are tolerant of modification and which ones are conserved. Furthermore, detailed knowledge of how the polypeptide's structure relates to its function is required. The specification does not disclose any information about the critical structural elements within the

nucleic acid molecules encoding the polypeptide of SEQ ID NO: 2 that are required to maintain the desired function such as the catalytic domain, the binding domain, and the like. No information has been provided as to which amino acid substitutions can be made without loss of activity. In the instant case, no examples of polynucleotides encoding the naturally occurring allelic variants of the polypeptide of SEQ ID NO: 2 with the desired function are provided either.

As described previously, the current state of the art clearly indicate that small amino acid changes can drastically change the function of a polypeptide. Furthermore, sequence identity alone is insufficient to accurately predict function (see Van de Loo et al. and Broun et al.). Therefore, due to the lack of relevant examples, the amount of information provided, the lack of knowledge about the critical structural elements required to maintain the desired function, and the unpredictability of the prior art in regard to function based on homology, one of ordinary skill in the art would have to go through the burden of undue experimentation in order to screen and isolate the naturally occurring allelic variants of the polypeptide of SEQ ID NO: 2 with the desired activity. Thus, Applicant has not provided sufficient guidance to enable one of ordinary skill in the art to make and use the invention in a manner reasonably correlated with the scope of the claims.

16. Claim 5 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the nucleic acid molecule of SEQ ID NO: 1 and the polypeptide of SEQ ID NO: 2, does not reasonably provide enablement for any nucleic acid which is at least 60% homologous to the nucleic acid molecule of SEQ ID NO: 1, any fragment of at least 200 nucleotides of a nucleic acid comprising the nucleotide sequence of SEQ ID NO: 1, any nucleic

acid molecule which encodes a polypeptide comprising an amino acid sequence at least 60% homologous to the amino acid SEQ ID NO: 2, and any nucleic acid molecule which encodes a fragment of at least 15 contiguous amino acid residues of the amino acid sequence of SEQ ID NO: 2. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The criteria for undue experimentation, summarized in *re Wands*, 8, USPQ2nd 1400 (Fed. Cir. 1988) are: 1) quantity of experimentation necessary, 2) the amount of direction or guidance presented, 3) the presence and absence of working examples, 4) the nature of the invention, 5) the state of prior art, 6) the relative skill of those in the art, 7) the predictability or unpredictability of the art, and 8) the breath of the claims.

Since the amino acid sequence of a polypeptide determines its structural and functional properties, predictability of which changes can be tolerated in a polypeptide's amino acid sequence to obtain the desired activity requires knowledge of and guidance with regard to which amino acids, if any, are tolerant of modification and which ones are conserved. Furthermore, detailed knowledge of how the polypeptide's structure relates to its function is required. The specification does not disclose any information about the critical structural elements within the nucleic acid molecules encoding the polypeptide of SEQ ID NO: 2 or the nucleic acid molecule of SEQ ID NO: 1 that are required to maintain the desired function such as the catalytic domain, the binding domain, and the like. No information has been provided as to which amino acid substitutions can be made without loss of kinase activity. In the instant case, no examples of (1) polynucleotides at least 60% homologous to the nucleic acid molecule of SEQ ID NO: 1, (2)

fragments of at least 200 nucleotides of a nucleic acid comprising the nucleotide sequence of SEQ ID NO: 1, (3) polynucleotides encoding a polypeptide comprising an amino acid sequence at least 60% homologous to the amino acid SEQ ID NO: 2, and (4) polynucleotides encoding fragments of at least 15 contiguous amino acid residues of the amino acid sequence of SEQ ID NO: 2 with the desired function are provided either.

As described previously, the current state of the art clearly indicate that small amino acid changes can drastically change the function of a polypeptide. Furthermore, sequence identity alone is insufficient to accurately predict function (see Van de Loo et al. and Broun et al.). Therefore, due to the lack of relevant examples, the amount of information provided, the lack of knowledge about the critical structural elements required to maintain the desired function, and the unpredictability of the prior art in regard to function based on homology, one of ordinary skill in the art would have to go through the burden of undue experimentation in order to screen and isolate (1) polynucleotides at least 60% homologous to the nucleic acid molecule of SEQ ID NO: 1, (2) fragments of at least 200 nucleotides of a nucleic acid comprising the nucleotide sequence of SEQ ID NO: 1, (3) polynucleotides encoding a polypeptide comprising an amino acid sequence at least 60% homologous to the amino acid SEQ ID NO: 2, and (4) polynucleotides encoding fragments of at least 15 contiguous amino acid residues of the amino acid sequence of SEQ ID NO: 2 which have the desired activity. Thus, Applicant has not provided sufficient guidance to enable one of ordinary skill in the art to make and use the invention in a manner reasonably correlated with the scope of the claims.

Claim Rejections - 35 USC § 102

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

17. Claims 5 and 6 (claims 7-12 and 22 dependent thereon) are rejected under 35 U.S.C. 102(a) as being anticipated by Berlanga et al. (Eur. J. Biochem. 265:754-762, 1999; EMBL accesion numbers AJ243533 and AJ243428) and Duesterhoeft et al. (GenEMBL accession numbers AL137627 and AL157497). Berlanga et al. teaches the characterization of a mammalian homolog of the GCN2 eukaryotic initiation factor 2α kinase in mouse (AJ243533) and human (AJ243428). The nucleic acid molecule encoding the mouse homolog presents 70.8% sequence homology to the nucleic acid molecule of SEQ ID NO: 1. The human homolog comprises a fragment of 2161 amino acid residues with 100% sequence identity to SEQ ID NO: 2. Duesterhoeft et al. teaches a nucleic acid molecule (AL157497) with 60.3% sequence homology to SEQ ID NO: 1 and comprises a fragment of 3332 nucleotides with 100% sequence homology to SEQ ID NO: 1. Duesterhoeft et al. also teaches a nucleic acid molecule (AL137627) comprising a fragment of 1082 nucleotides with 100% sequence homology to SEQ ID NO: 1 (see attached alignments). Therefore, as written, claim 5 is anticipated by Berlanga et al. (AJ243533) and by Duesterhoeft et al. (AL157497) because their molecules are at least 60% homologous to SEQ ID NO: 1 (5(a)), comprise at least 200 nucleotides of SEQ ID NO: 1 (5(b)), encode a polypeptide at least 60% homologous to SEQ ID NO: 2 (5(c)), and encode a polypeptide comprising at least 15 contiguous amino acid residues of SEQ ID NO: 2. In addition, as written, claim 5(b) and 5(d) are anticipated by Berlanga et al. (AJ243428) and by Duesterhoeft et al. (AL AL137627) because their molecules comprise at least 200 nucleotides of SEQ ID NO: 1 and encode a fragment of at least 15 contiguous amino acid residues of SEQ ID

NO: 2. Claim 6, as written, is also anticipated since any of the molecules taught by Berlanga et al. or Duesterhoeft et al. can hybridize to the molecules of any of claims 1 through 5. It is noted that the molecules of Berlanga et al. and Duesterhoeft et al. mentioned above are disclosed by Applicant as prior art in Figure 2 and BLAST alignment in IDS, respectively

Allowable Subject Matter

18. Claim 2 is allowed.

19. The following is an examiner's statement of reasons for allowance: The closest homolog of the nucleic acid molecule encoding the polypeptide of SEQ ID NO: 2 presents 70.8% sequence identity (Berlanga et al., GenEMBL accession number AJ243533, October 1999) to the nucleic acid molecule of claim 2. Therefore, no applicable prior art has been found for the nucleic acid molecule encoding the polypeptide of SEQ ID NO: 2. Further, the prior art does not teach or suggest preparing the claimed nucleic acid sequences specifically, therefore nucleic acid molecules comprising the nucleic acid sequence encoding the polypeptide of SEQ ID NO: 2 are new and non-obvious.

Certain papers related to this application may be submitted to Art Unit 1652 by facsimile transmission. The FAX number is (703) 308-4556. The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 CFR 1.6(d)). NOTE: If Applicant submits a paper by FAX, the original copy should be retained by Applicant or Applicant's representative. NO DUPLICATE

COPIES SHOULD BE SUBMITTED, so as to avoid the processing of duplicate papers in the Office.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Delia M. Ramirez whose telephone number is (703) 306-0288. The examiner can normally be reached on Monday-Friday from 8:30 AM to 5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Ponnathapura Achutamurthy can be reached on (703) 308-3804. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Delia M. Ramirez, Ph.D.
Patent Examiner
Art Unit 1652

DR
November 13, 2001

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